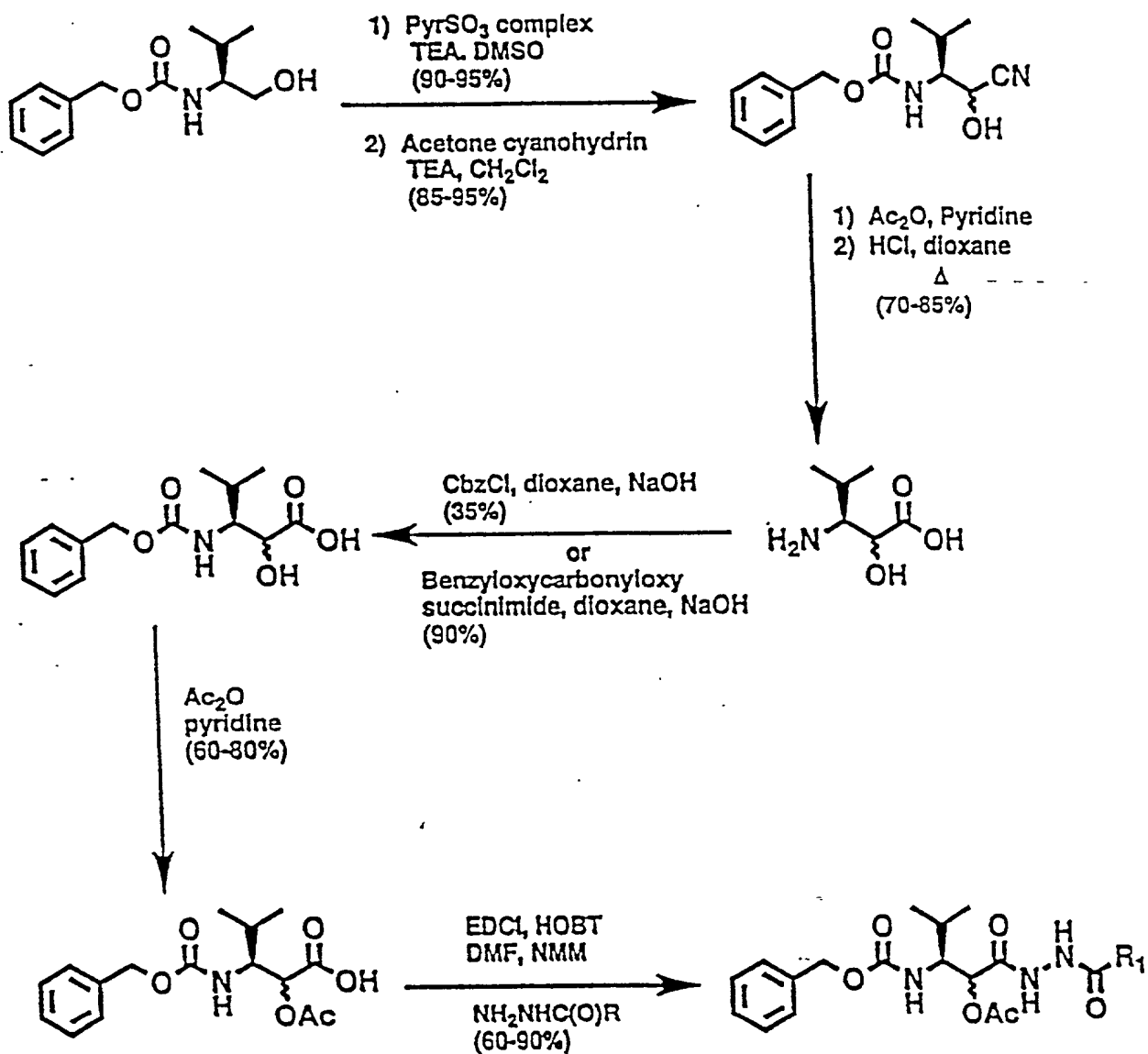


Figure 1

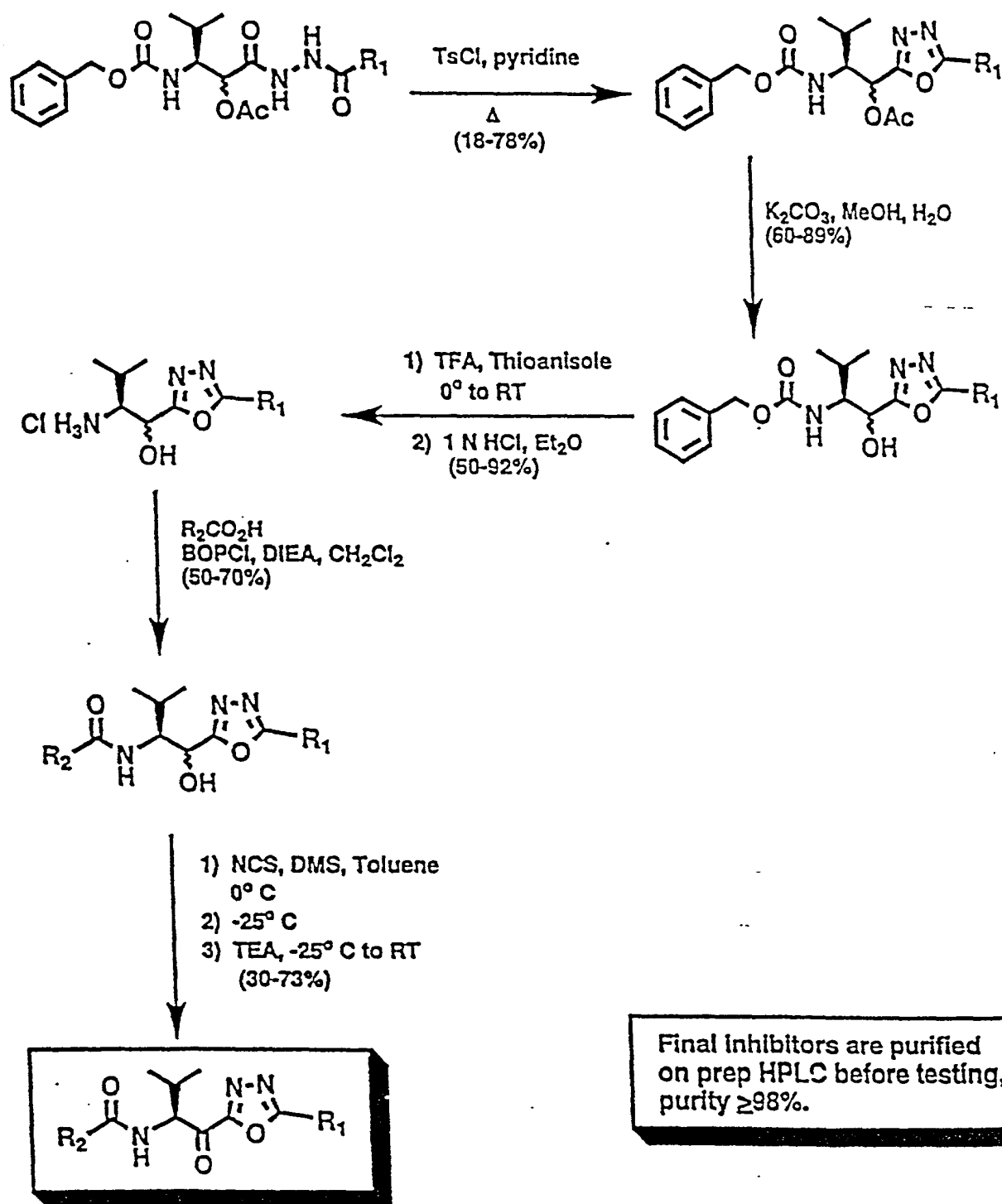
General Synthetic Scheme for 1,3,4-Oxadiazole Inhibitors



T00T80' 22922660

Figure 2

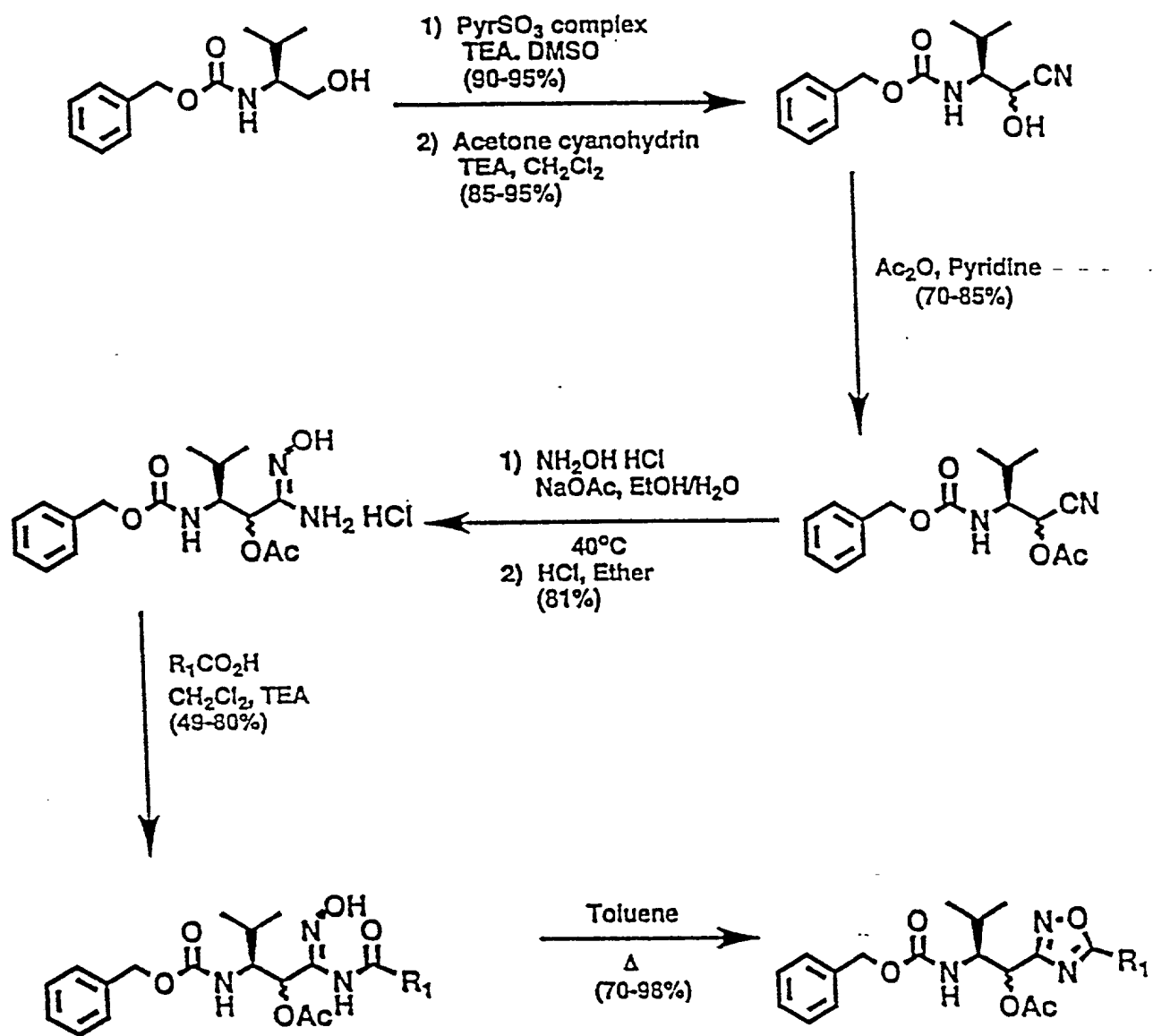
General Scheme for 1,3,4-Oxadiazole Inhibitors - Continued



T00180" 22242660

Figure 3

General Synthetic Scheme for 1,2,4-Oxadiazole Inhibitors



05927833-034001

Figure 4

General Synthetic Scheme for 1,2,4-Oxadiazole inhibitors
(Continued)

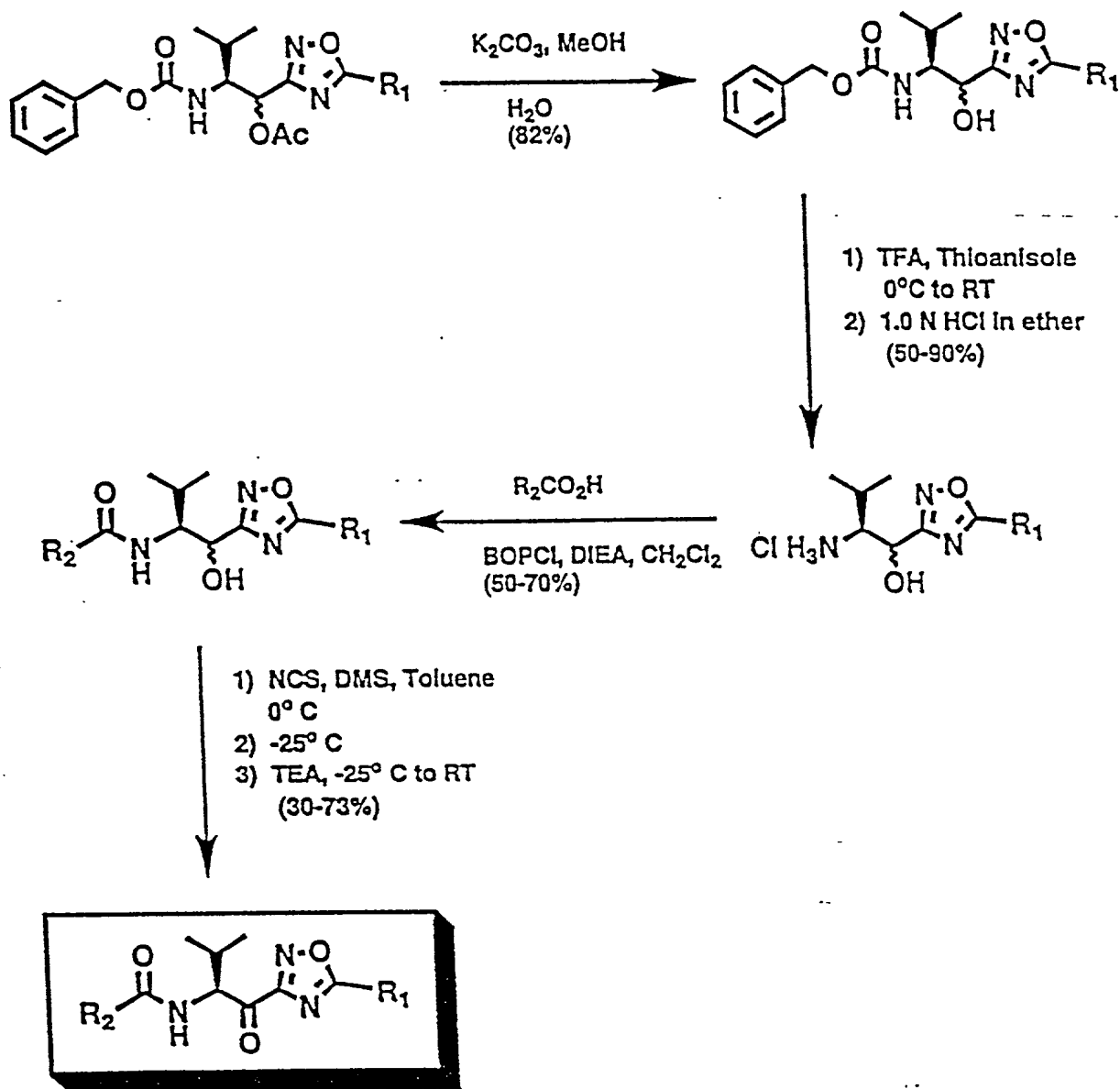


Figure 5

General Synthetic Scheme for P₂-P₃ Modified Based Inhibitors

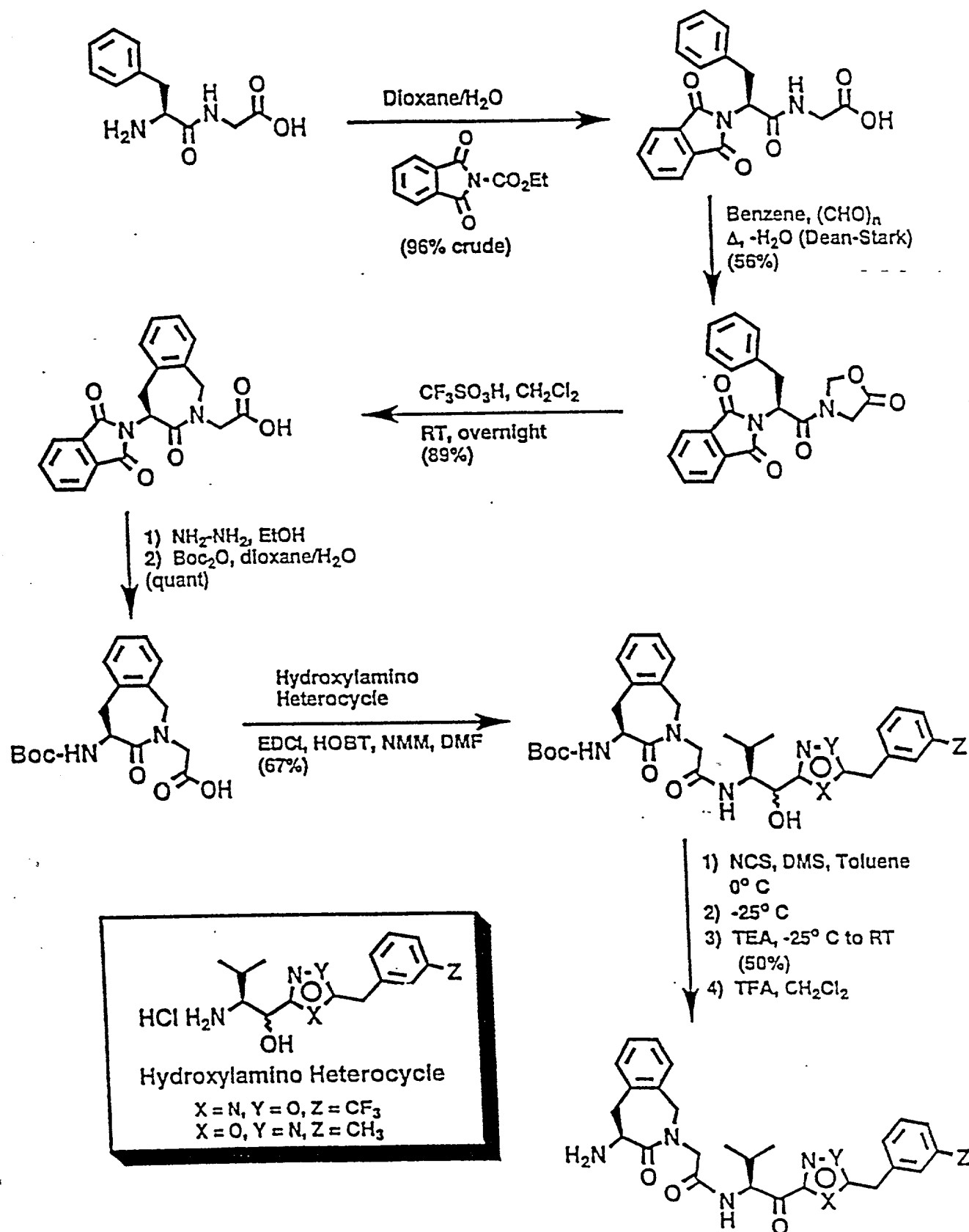


Figure 6

Synthetic Scheme for P₂-P₃ Modified Inhibitors

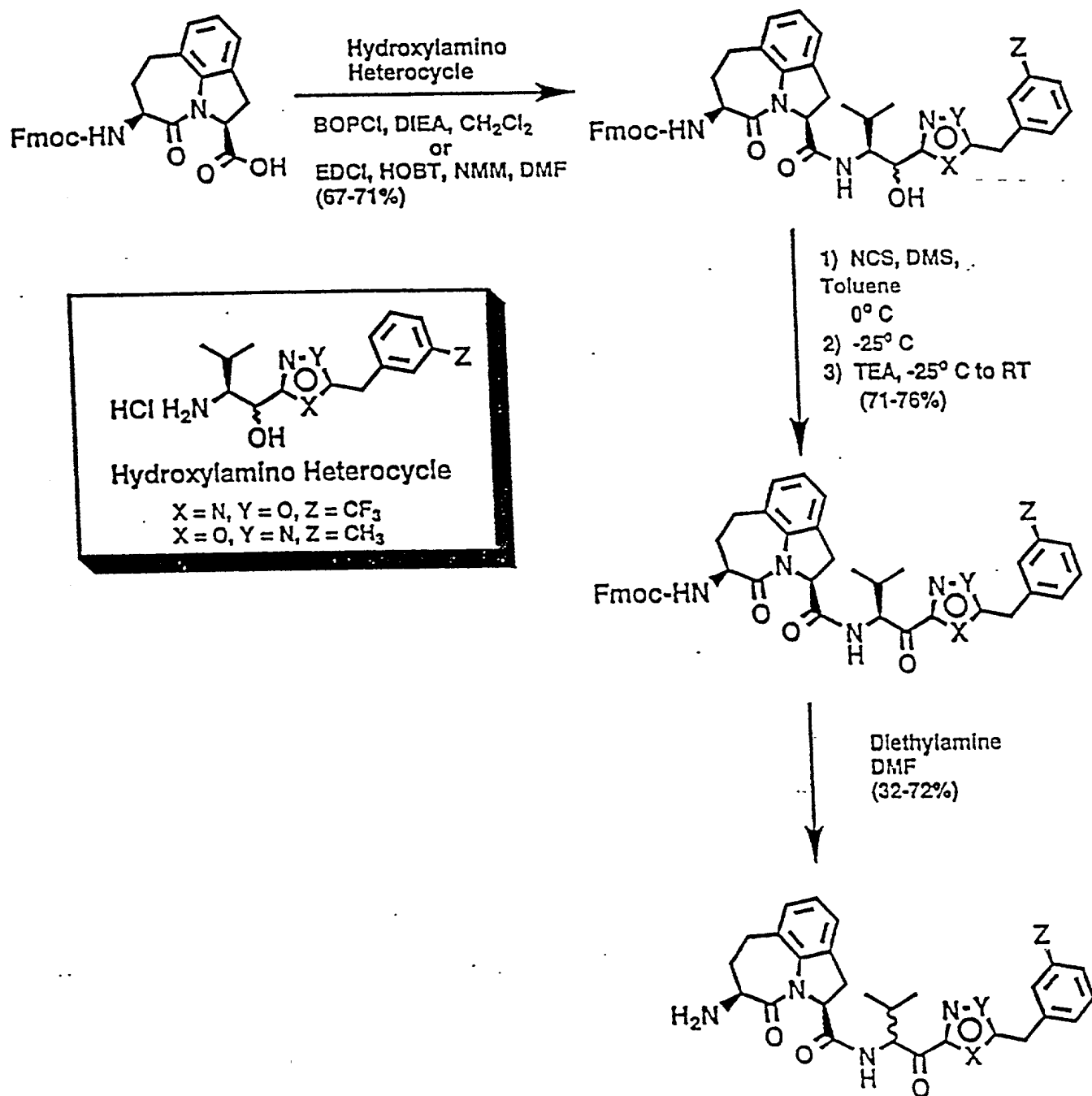
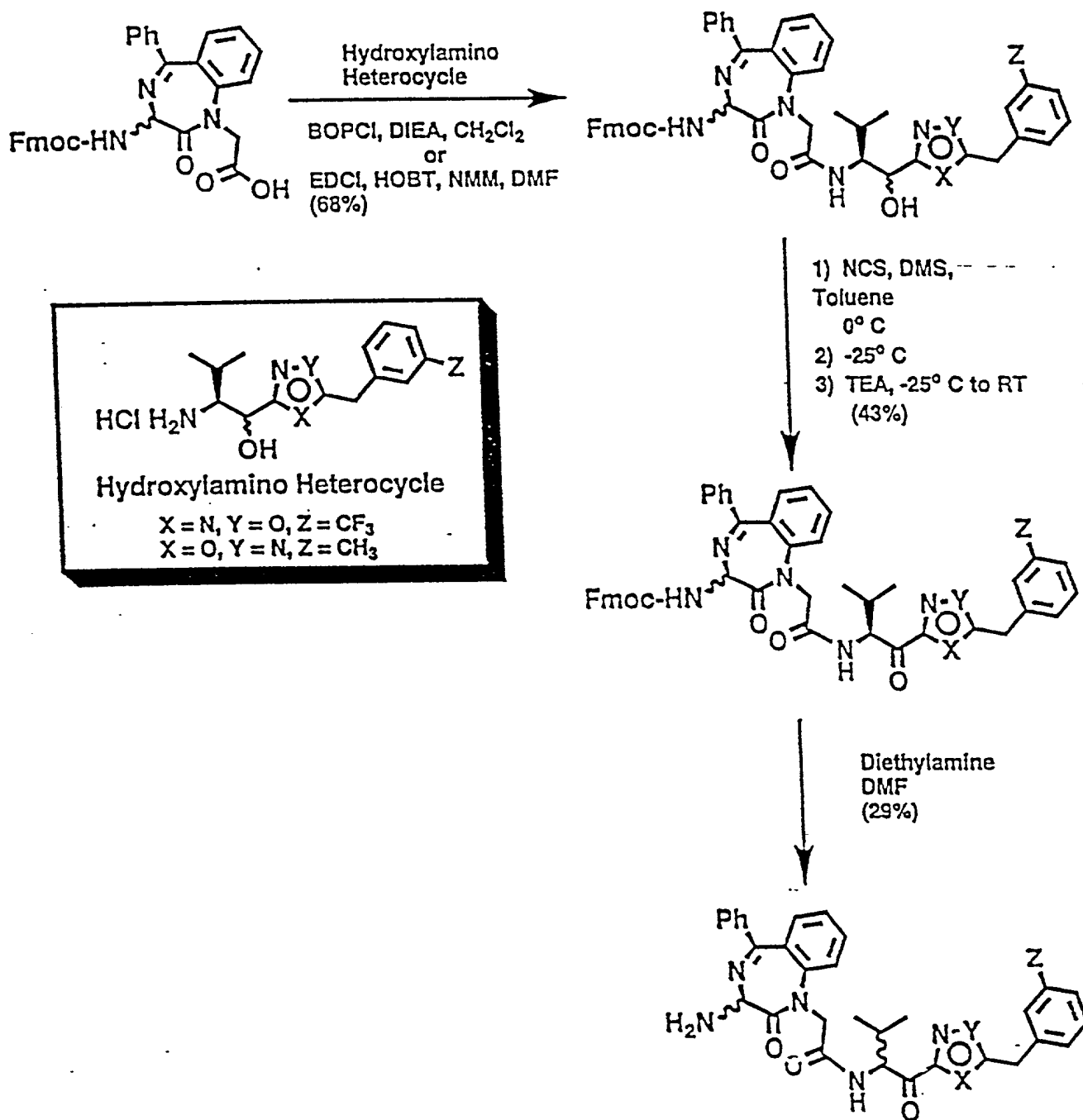


Figure 7

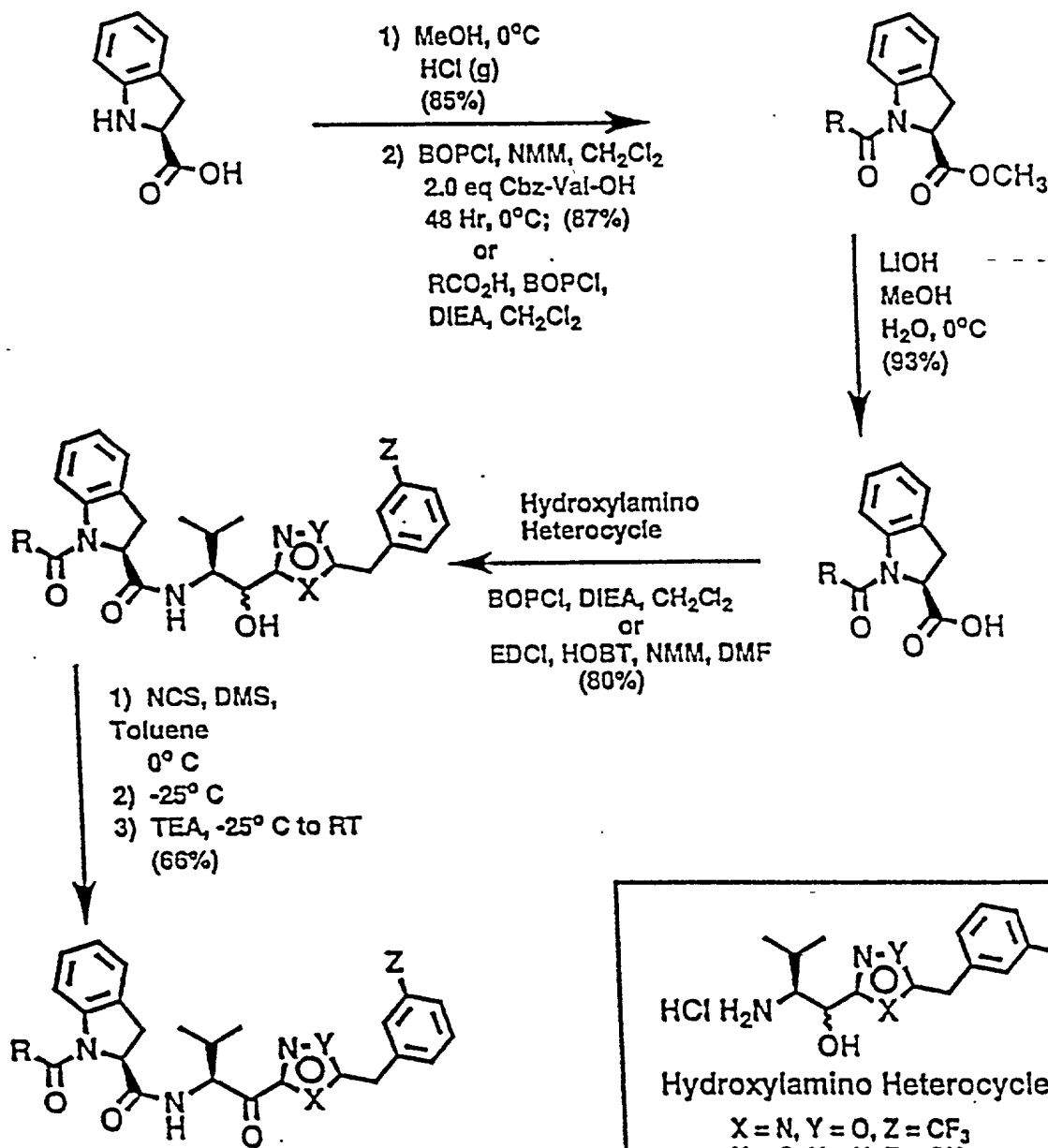
Synthetic Scheme for P₂-P₃ Modified Inhibitors



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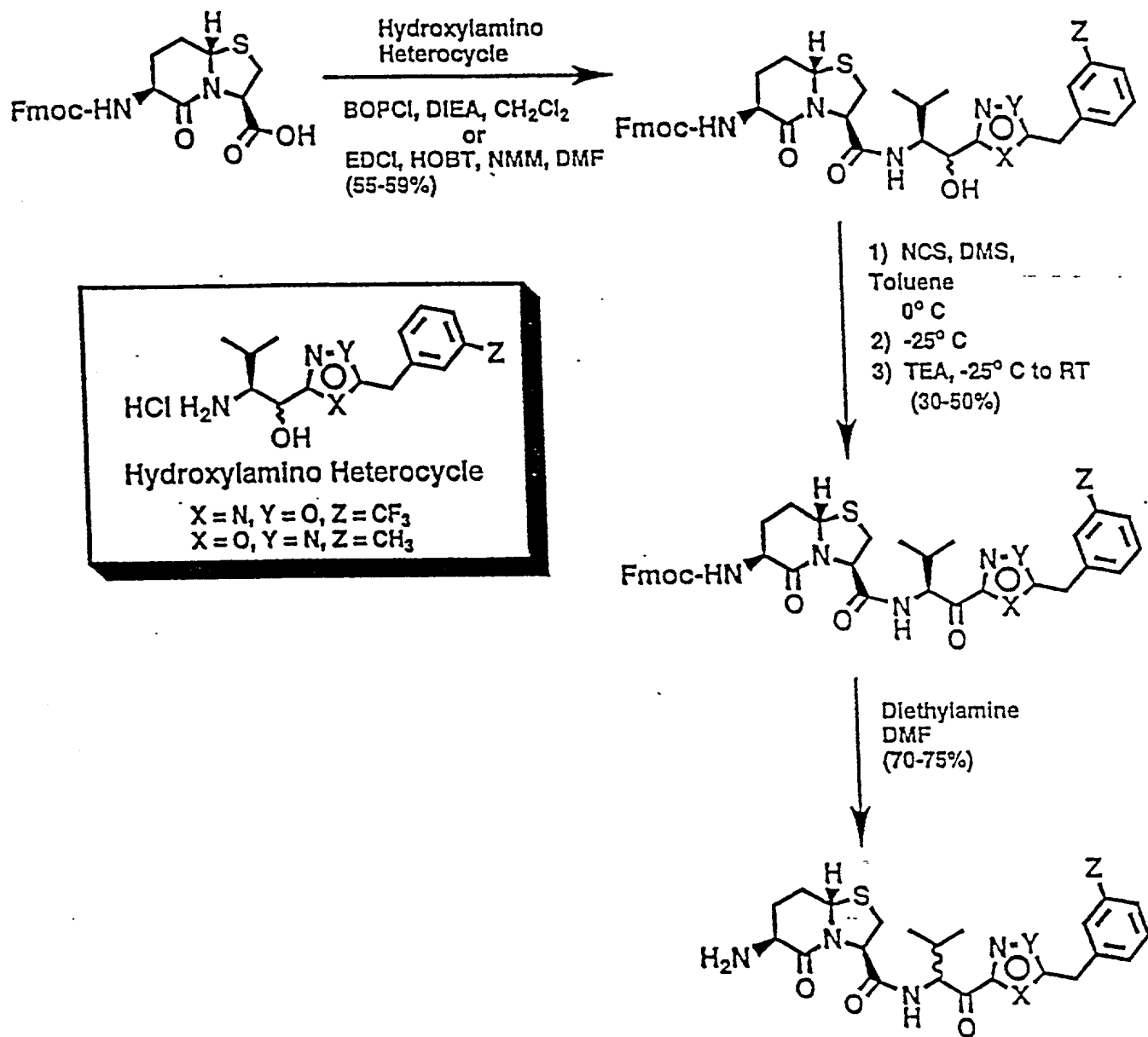
Figure 8

General Synthetic Scheme for P₂-P₃ Modified Inhibitors



T00180-228/2260

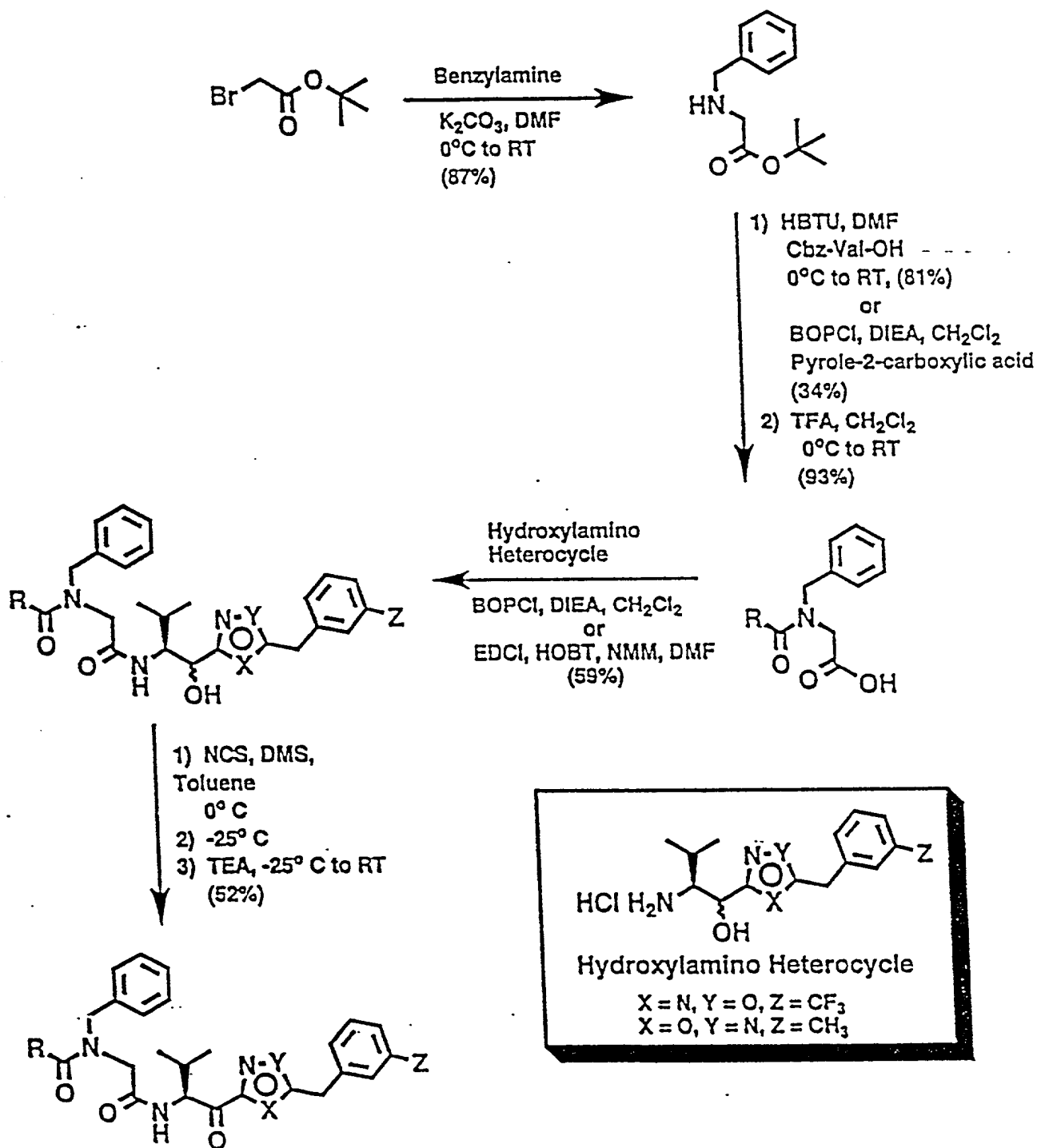
Figure 9

Synthetic Scheme for P₂-P₃ Modified Inhibitors

T0927032-031001

Figure 10

General Synthetic Scheme for P₂-P₃ Modified Inhibitors



T0927833-031001

Figure 11

General Synthetic Scheme for P₂-P₃ Lactam Based Inhibitors

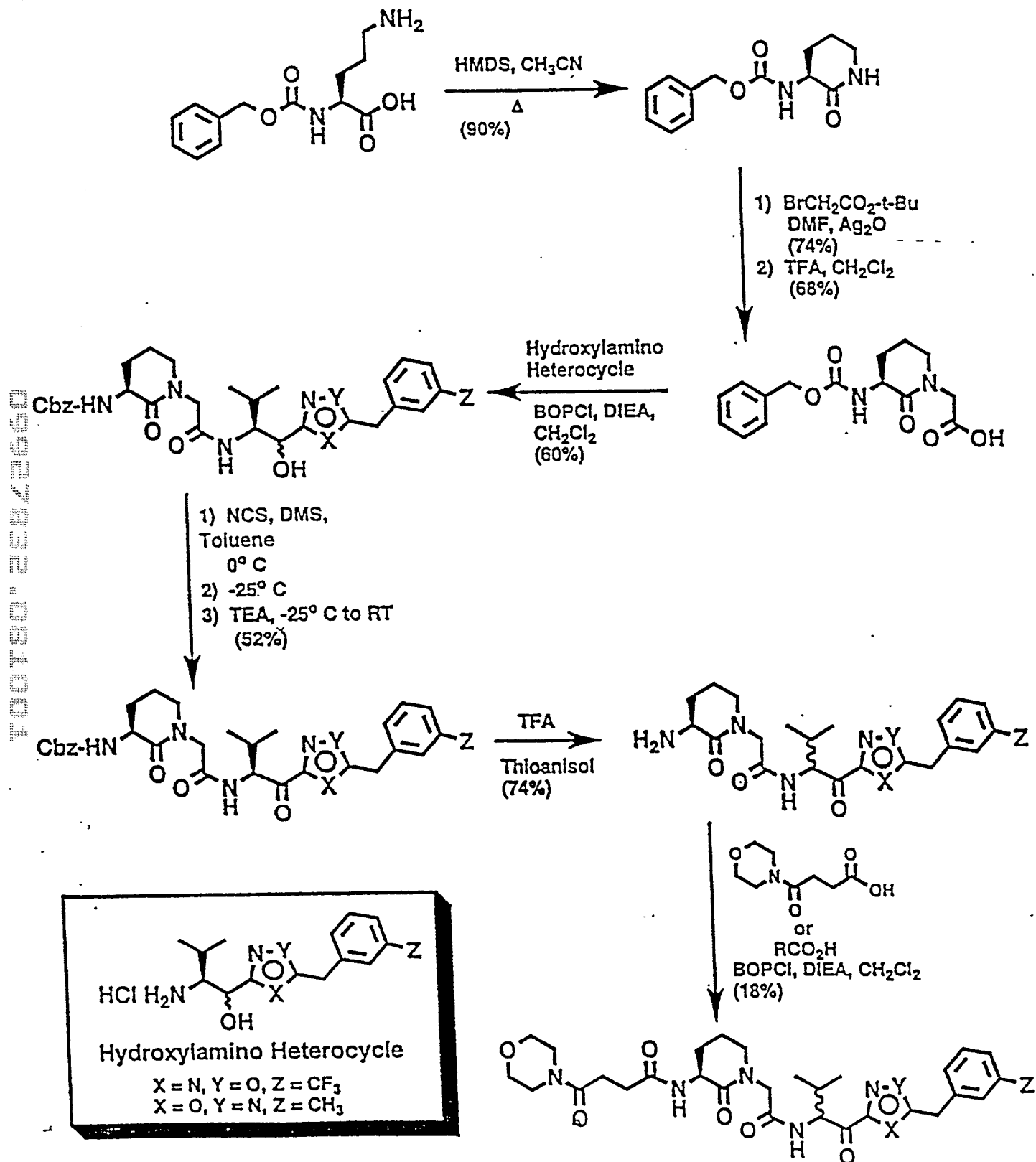
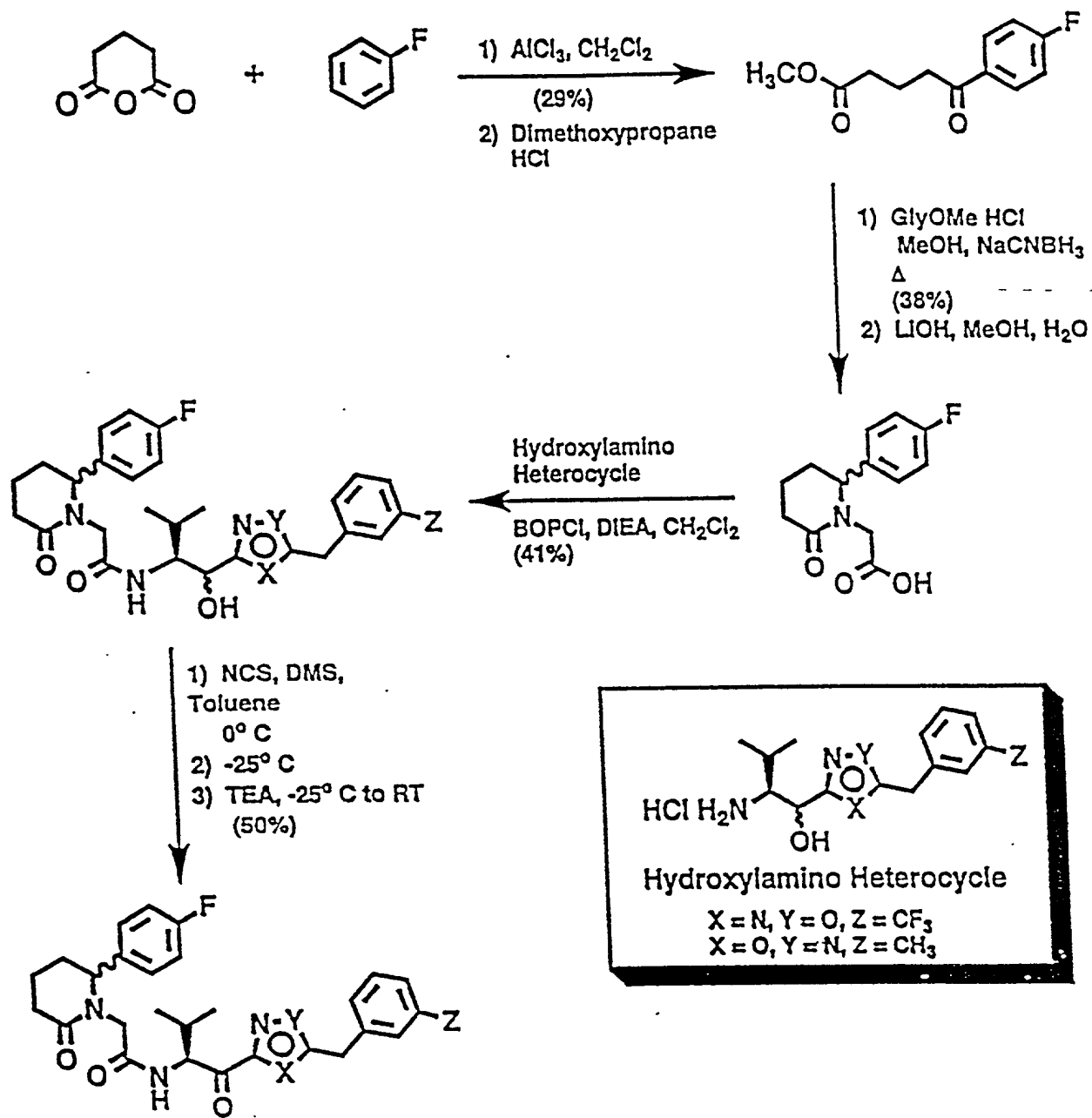


Figure 12

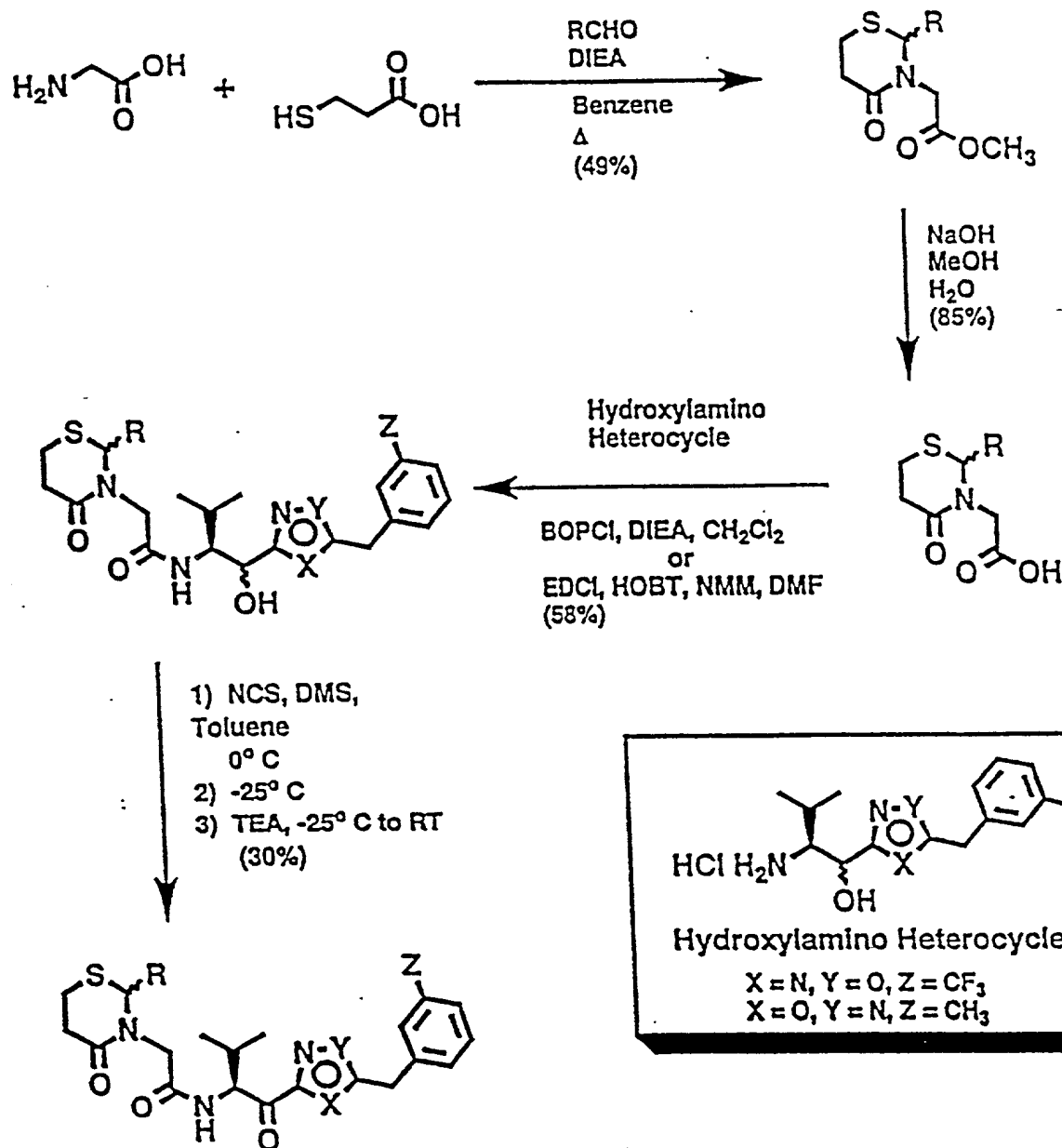
General Synthetic Scheme for P₂-P₃ Lactam Based Inhibitors



T00760-2282550

Figure 13

General Synthetic Scheme for Metathiazanone Based Inhibitors



T00790-22242650

Figure 14

General Synthetic Scheme for Thiazolidinone Based Inhibitors

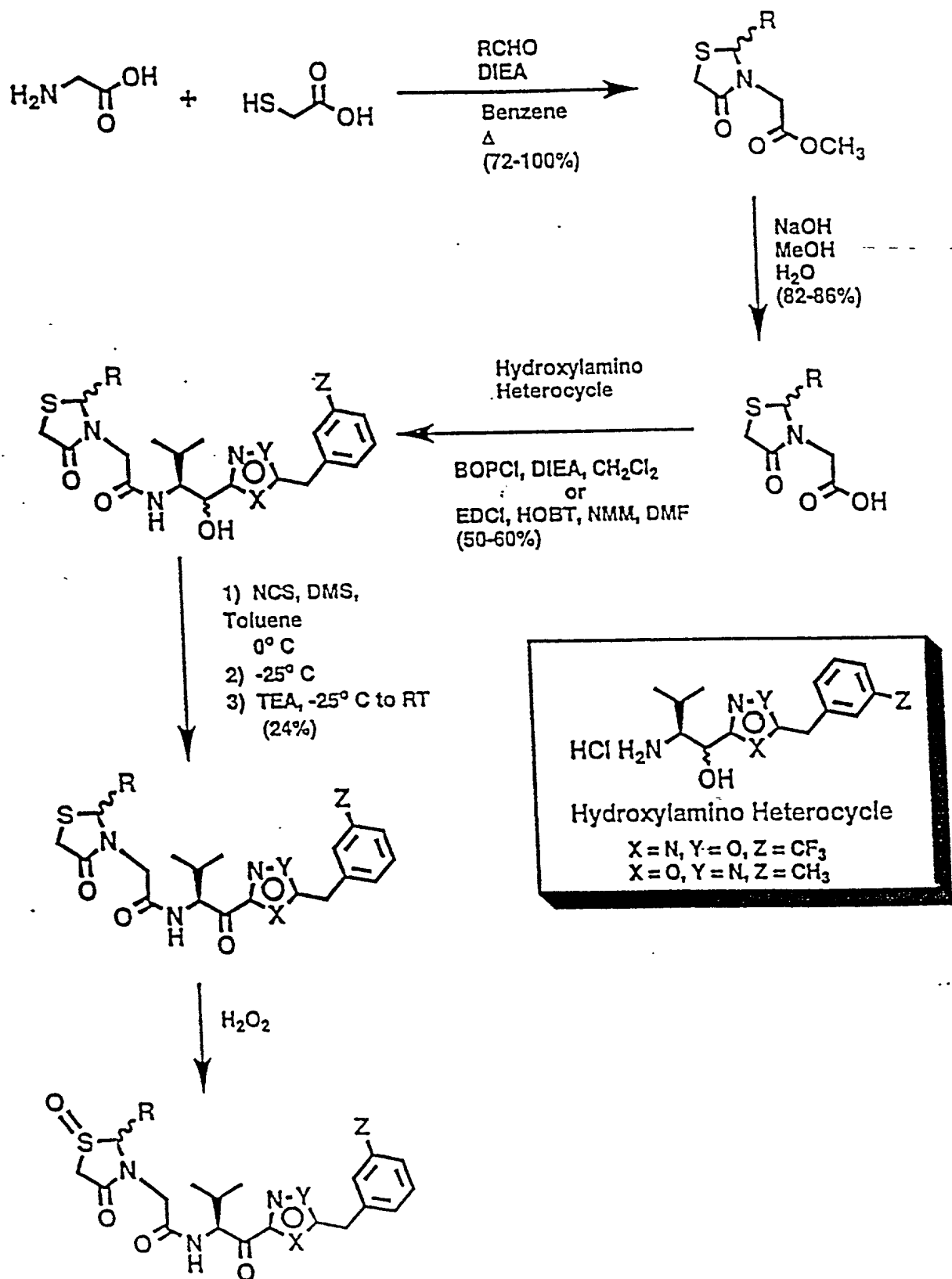


Figure 15

General Synthetic Scheme for Pyridazinedione Based Inhibitors

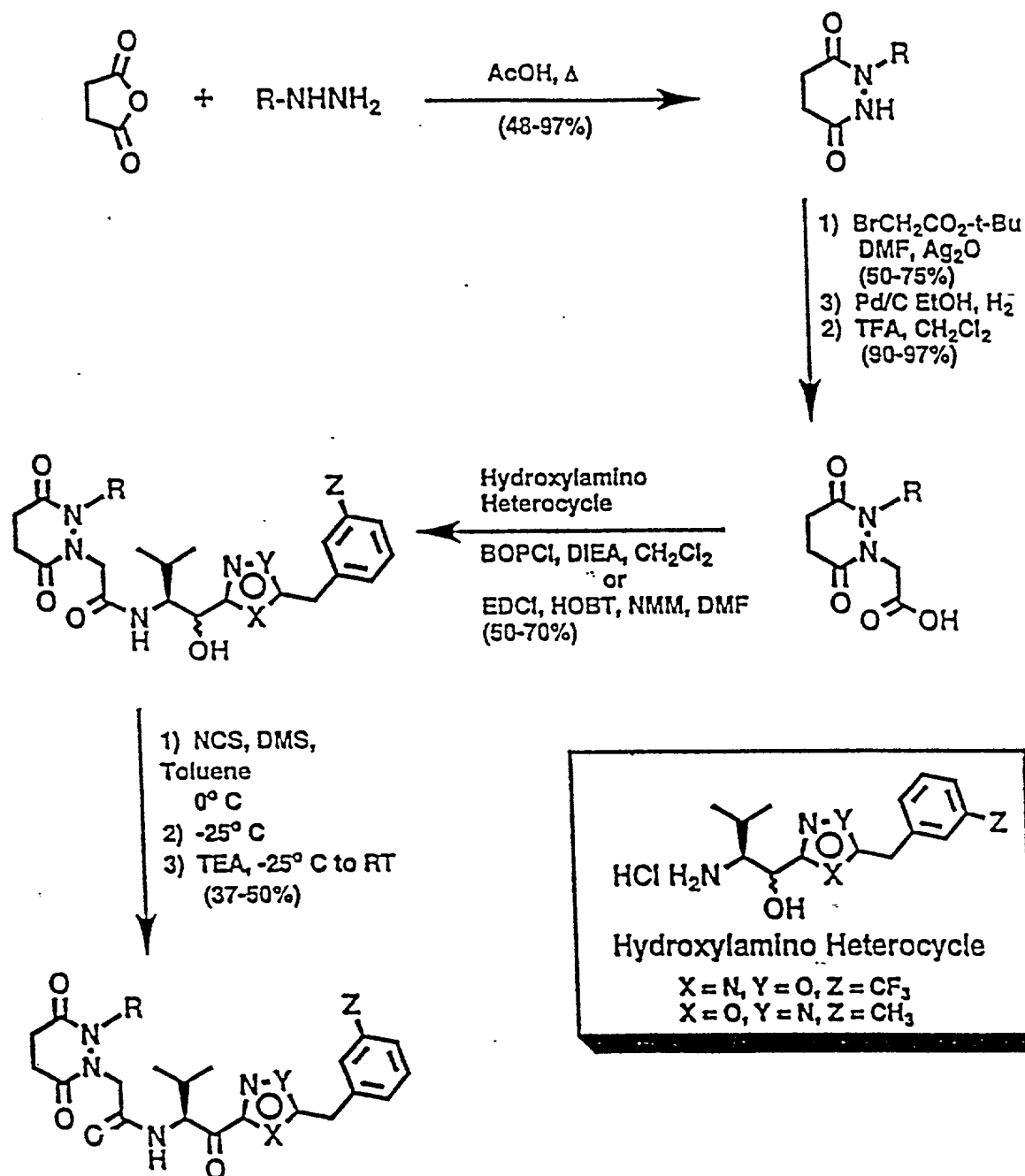
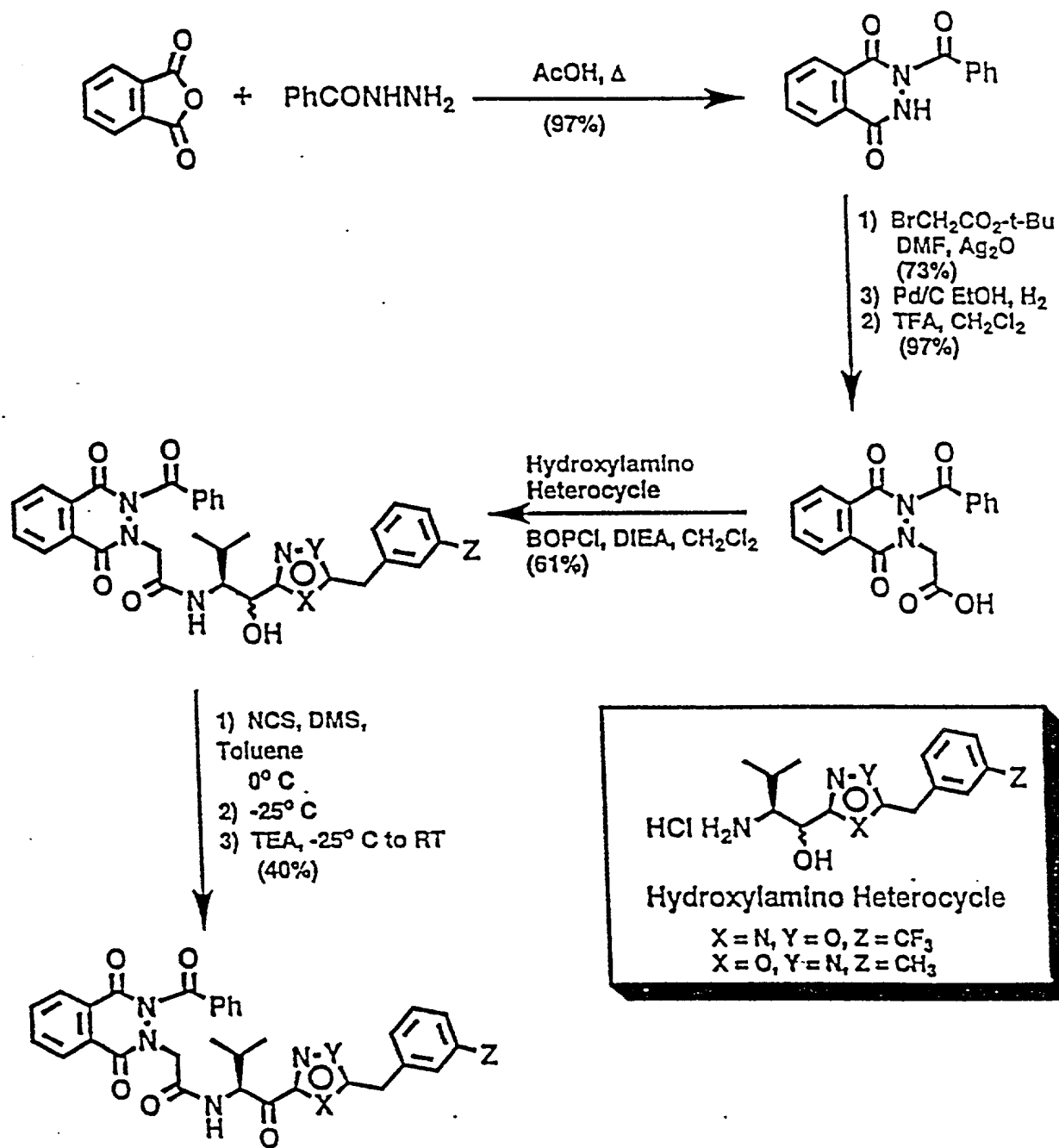


Figure 16

General Synthetic Scheme for Benzopyridazinedione Based Inhibitors



T03789-22942660

Figure 17

General Synthetic Scheme for Quinolone and N-Substituted Quinolone Based Inhibitors

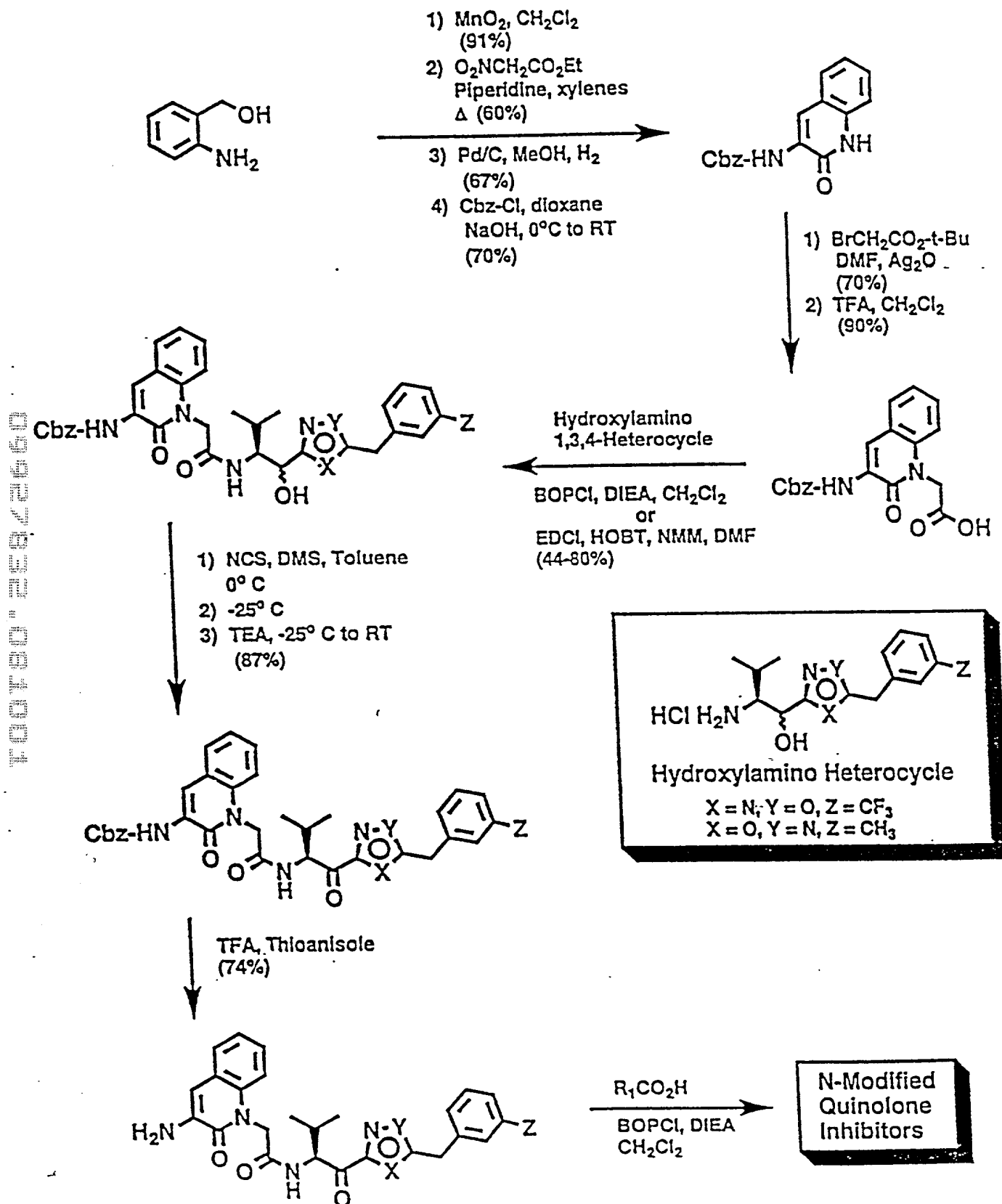
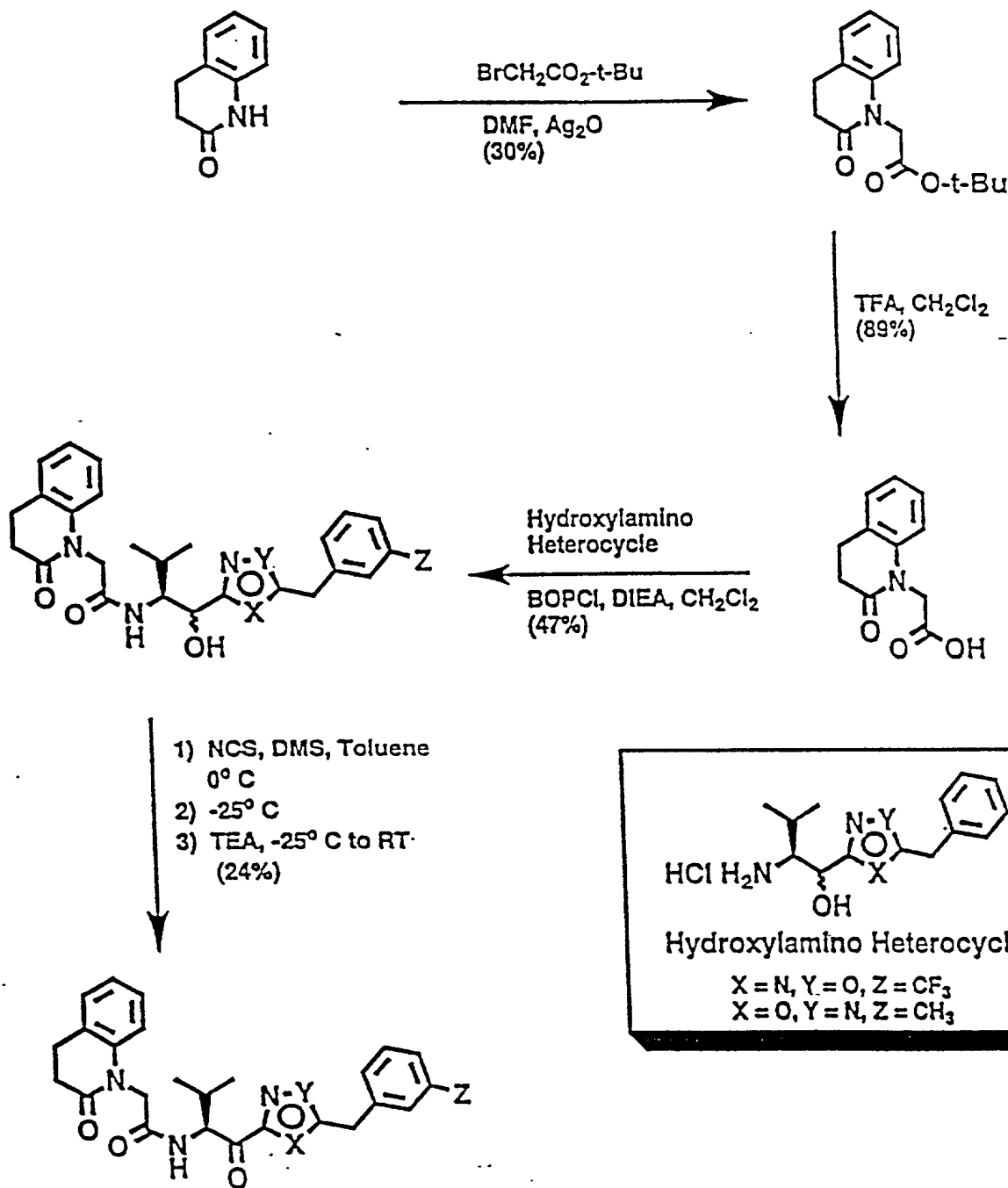


Figure 18

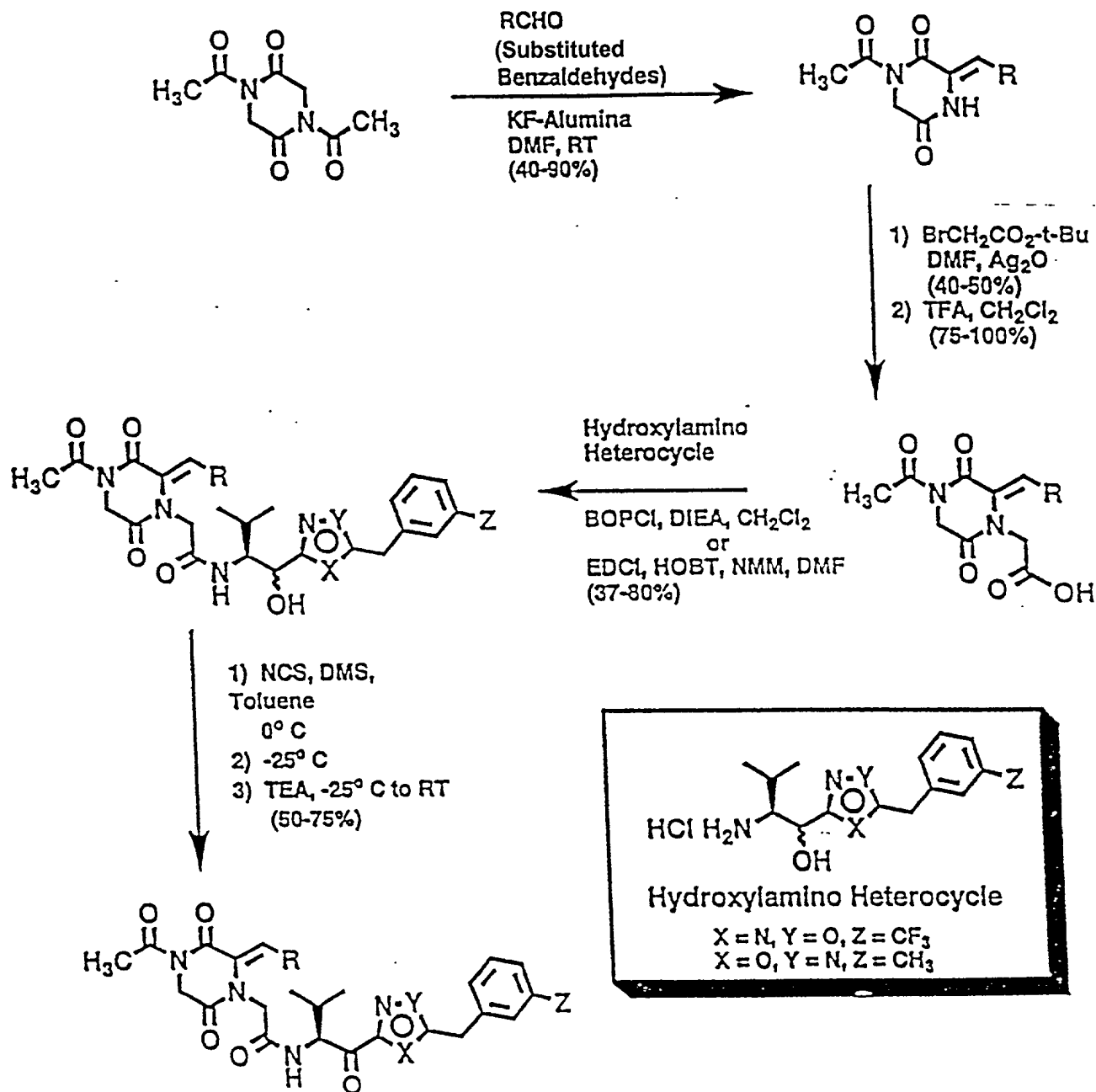
General Synthetic Scheme for 3,4-Dihydroquinolone Based Inhibitors



05927832-004001

Figure 19

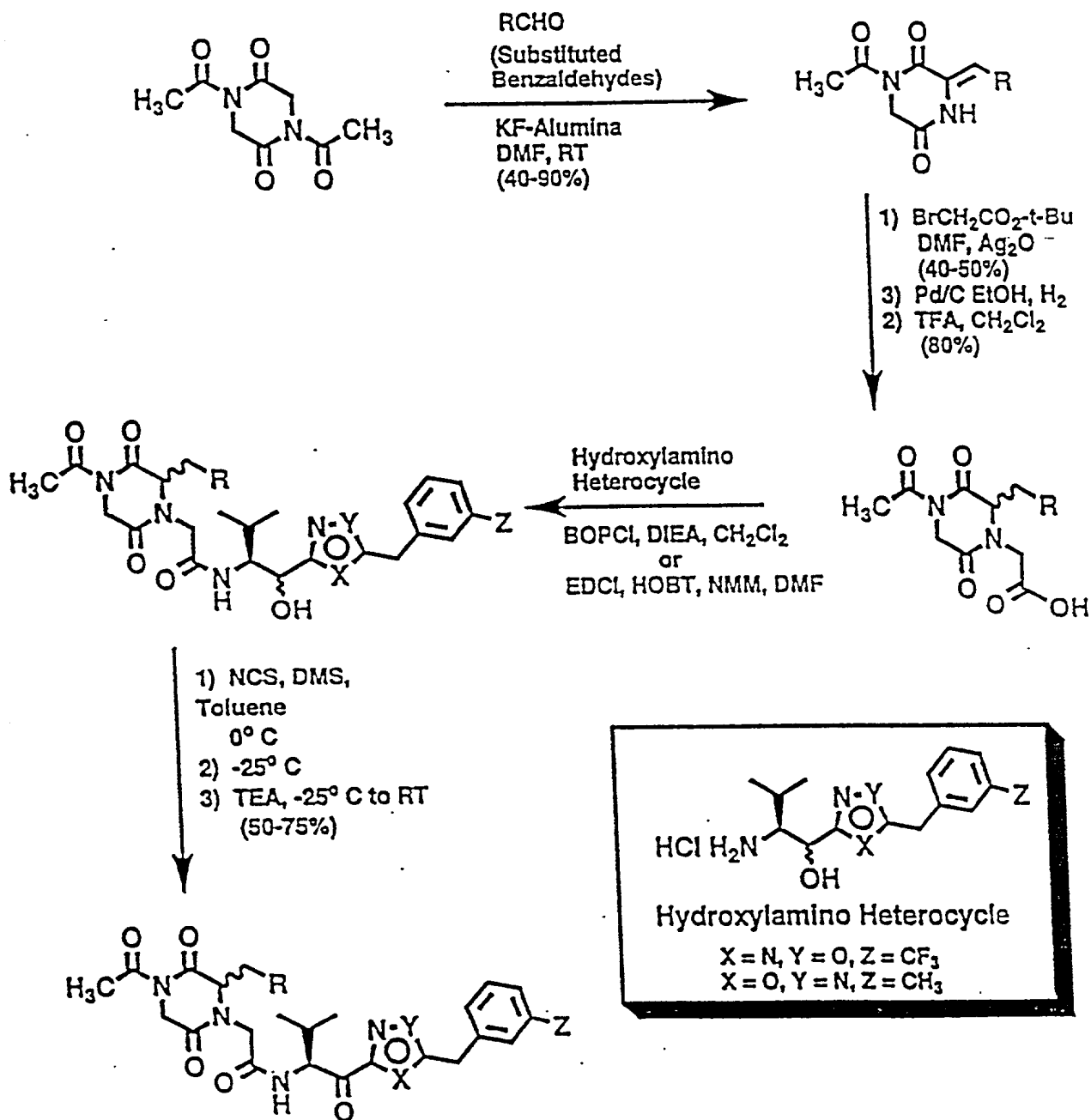
General Synthetic Scheme for Benzylidene Diketopiperazine Based Inhibitors



T0927833-081004

Figure 20

General Synthetic Scheme for Diketopiperazine Based Inhibitors



09927833-091001

Figure 21

Synthetic Scheme for Hydantoin Based Inhibitors

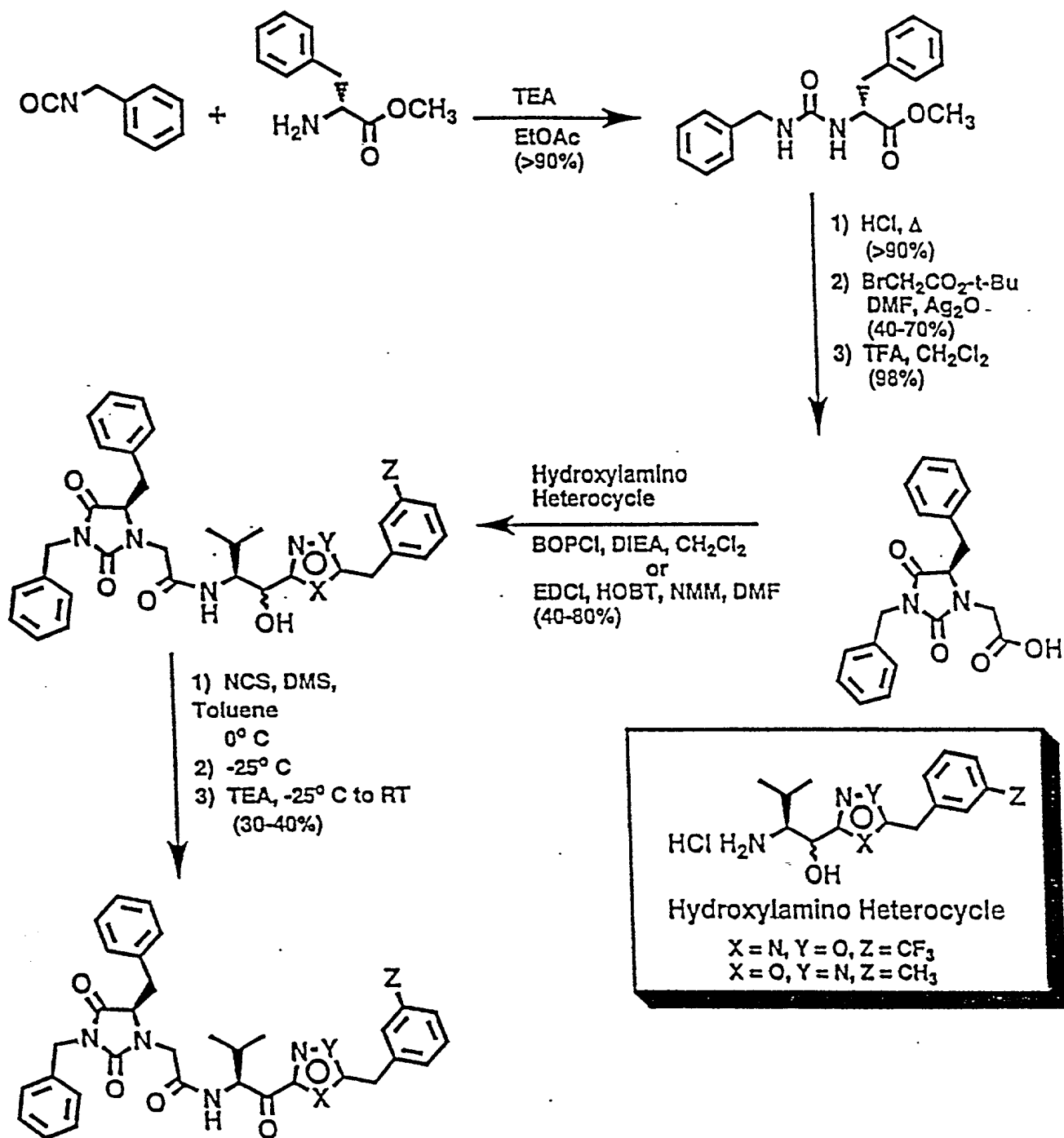
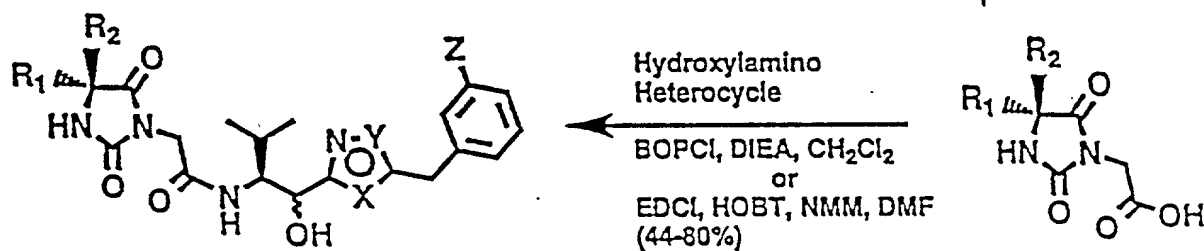
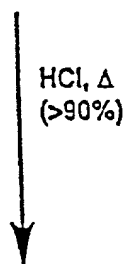
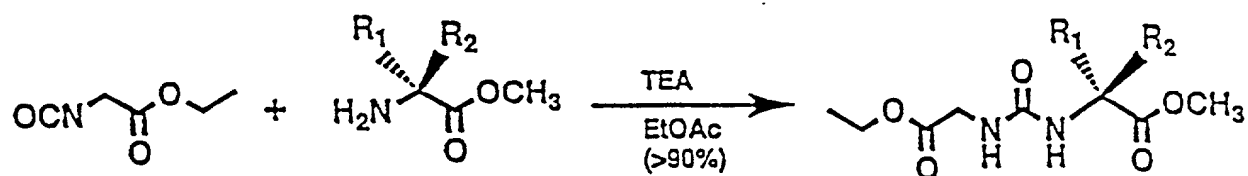
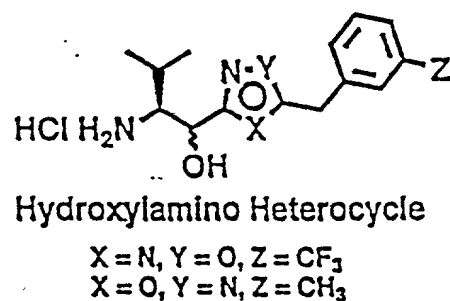
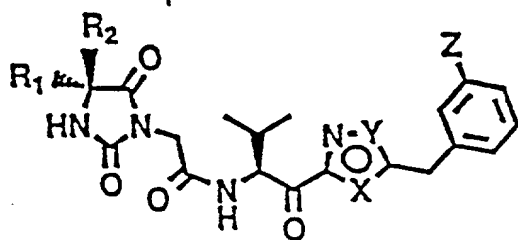


Figure 22

General Synthetic Scheme for Hydantoin Based Inhibitors

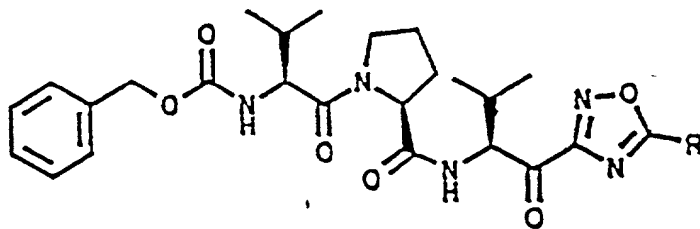


- 1) NCS, DMS, Toluene, 0° C
- 2) -25° C
- 3) TEA, -25° C to RT (30-45%)



T09780-2207650

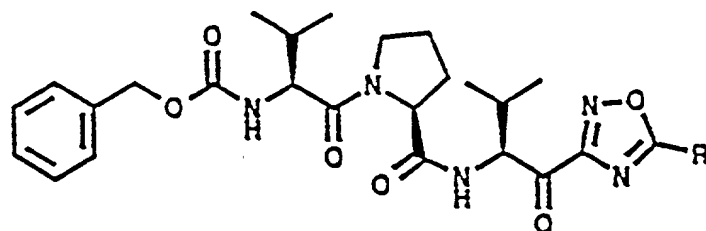
Figure 23



CE#	R	K _i (nM)	CE#	R	K _i (nM)
2039		2.0	2054		0.29
2042		2.5	2055		0.49
2045		1.0	2058		0.56
2048		0.36	2062		0.30
2049		0.5	2066		0.98
2052		0.37	2096		0.8
2053		0.41	2115		1.0

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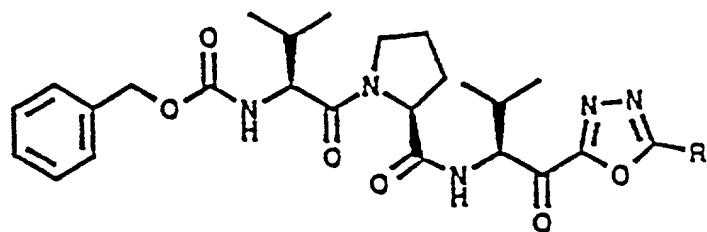
Figure 24



CE#	R	K _i (nM)	CE#	R	K _i (nM)
2046		9.9	2077		0.15
2047		3.8	2078		1.05
2050		1.84	2092		6.3
2057		0.38	2103		12.4
2069		4.4	2119		7.7
2073		0.24	2152		0.24
2076		1.46			

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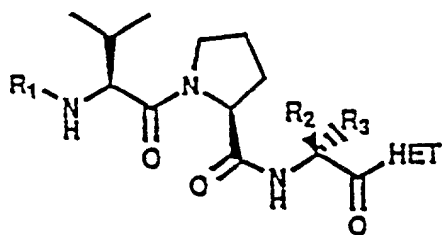
Figure 25



CE#	R	K_I (nM)
2072		0.025
2074	-CH ₃	0.99
2075		0.11
2100		0.069
2123	-N(CH ₃) ₂	15.1
2124		0.033

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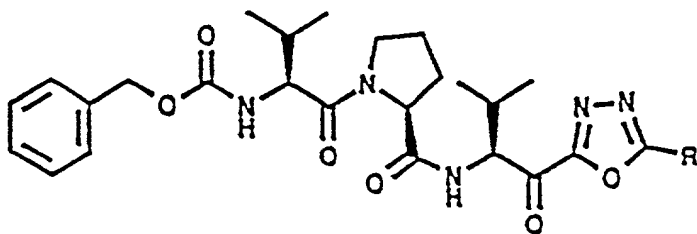
Figure 26



CE#	R ₁	R ₂	R ₃	HET	K _i (nM)
2083	Cbz-	CH ₃	CH ₃		73.0
2098		<i>L</i> -Propyl	H		85.0
2104		<i>L</i> -Propyl	H		0.33
2109		<i>L</i> -Propyl	H		126
2110		<i>L</i> -Propyl	H		0.13

20250709 22:23:25

Figure 27





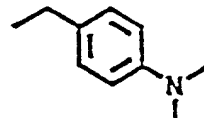

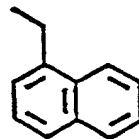
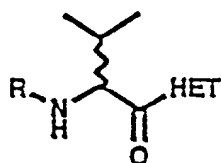
CE#	R	K _i (nM)
2072		0.025
2074	-CH ₃	0.99
2075		0.11
2100		0.069
2123		15.1
2124		0.033

Figure 28



CE#	R	HET	K_i (nM)
2130		B	10.0
2132		A	24.0
2134		B	2.0
2135		A	17
2126		B	5.05
2127		A	33.9

Heterocycles:

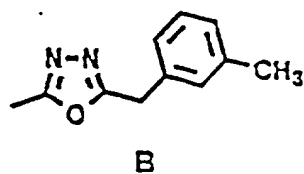
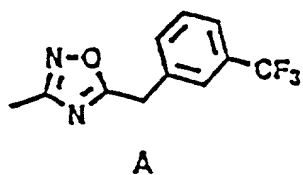
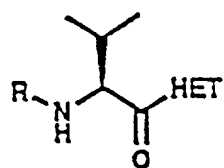
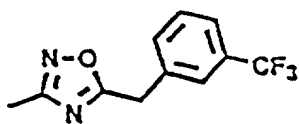


Figure 29

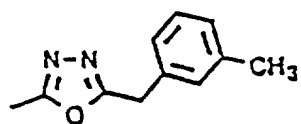


CE#	R	HET	K_i (nM)
2125		A	0.40
2145		B	0.038
2143		A	25.0
2056		A	0.98
2097		A	60.0
2156		A	512.0

Heterocycles:

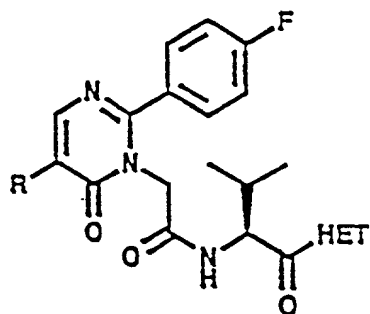


A



B

Figure 30



CE#	R	HET	K_i (nM)
2089	Cbz-NH-	A	1.5
2090	NH ₂ -	A	2.7
2095	Cbz-NH-	B	0.21
2101	NH ₂ -	B	0.64

Heterocycles:

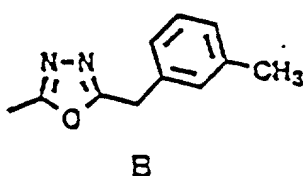
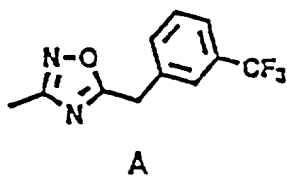
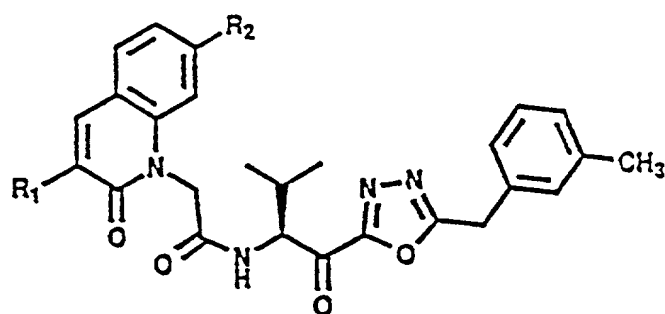
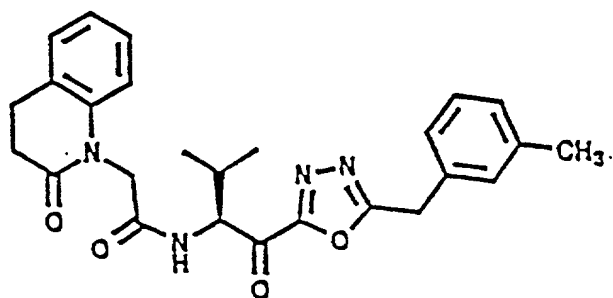


Figure 31

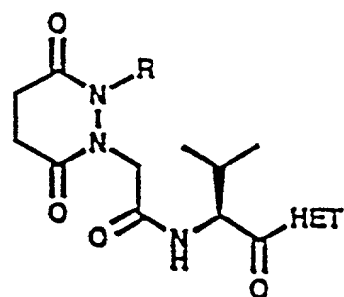


CE#	R ₁	R ₂	K _i (nM)
2107	Cbz-NH-		17.0
2108	Cbz-NH-	H	10.5
2113	H ₂ N-	H	38.8
2116		H	76.3
2117		F	587.0

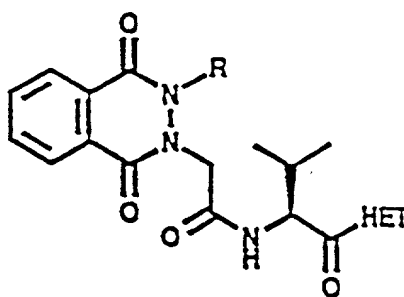


CE-2088 K_i = 66.0 nM

Figure 32



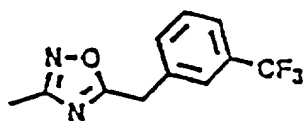
I



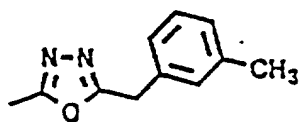
II

CE#	R	Structure	HET	K_i (nM)
2138		I	B	294.0
2147		I	B	1590
2148		I	A	>6000
2140		II	B	204.4

Heterocycles:

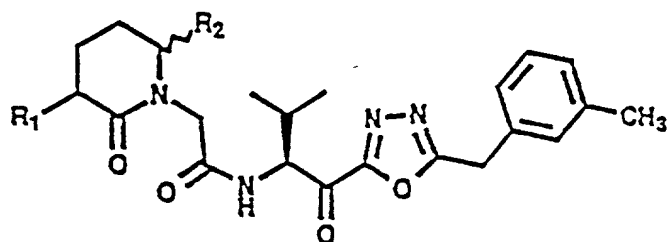



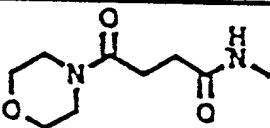
A



B

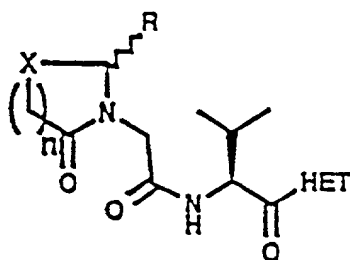
Figure 33



CE#	R ₁	R ₂	K _i (nM)
2079	Cbz-NH-	H	35.5
2080	H ₂ N-	H	62.0
2087	H		19.8
2091		H	270.0

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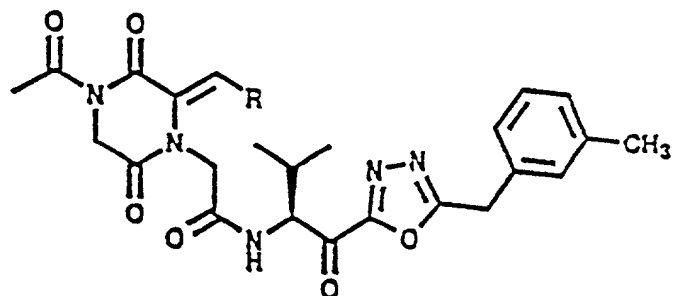
Figure 34


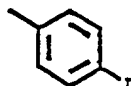
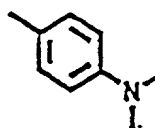

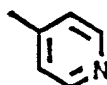


CE#	n	X	HET	R	K_i (nM)
2118	2	S			13.2
2121	1	S			28.0
2122	1	S			62.7
2136	1	SO			104.0
2137	1	SO			557.0

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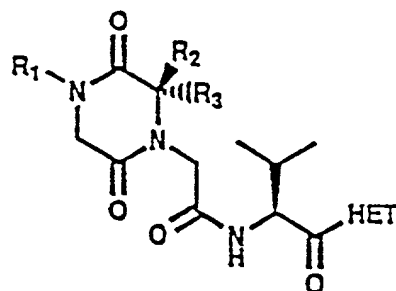
Figure 35



CE#	R	K_i (nM)
2099		1.9
2105		0.72
2111		20.1
2112		1.17
2114		25.1

2023032600

Figure 36



CE#	R ₁	R ₂	R ₃	HET	K _i (nM)
2084	CH ₃			A	133.0
2106	CH ₃			B	40.7
2120	CH ₃ CO-			B	50.9
2128		-H		B	64.0
2129		-H		A	300.3
2133		-H		C	33200
2139	H-			B	41.0
2144			-H	B	9.3
2146			-H	A	67.3

Heterocycles:

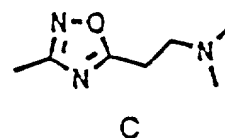
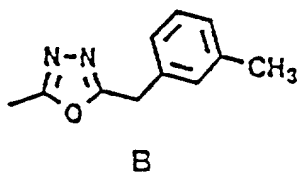
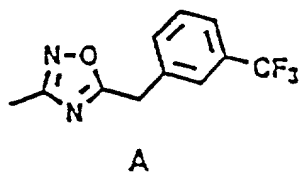
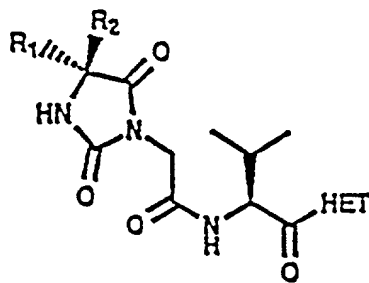


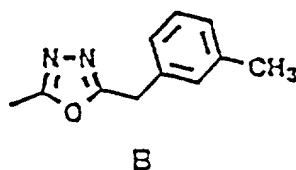
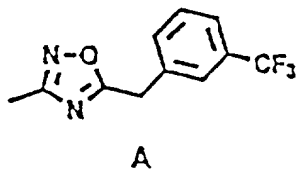
Figure 37

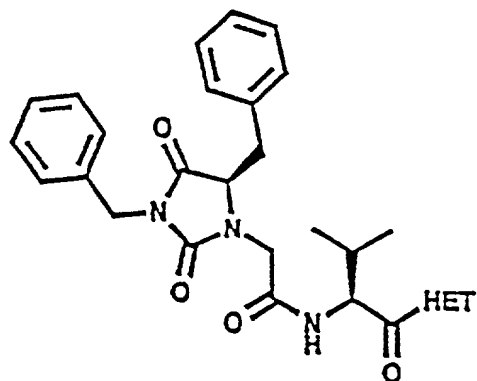


CE#	R ₁	R ₂	HET	K _i (nM)
2141		H	A	64.0
2142		H	B	8.7
2149 ^{**}		H	B	0.28
2154	H		B	10.0
2155	H		A	57.0

^{**} Stereochemistry not definitive

Heterocycles:



[illegible]

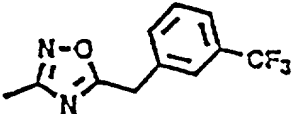
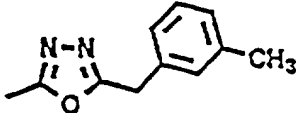
CE#	HET	K_I (nM)
2150		>1000
2151		60

Fig - Synthesis of ONO-PO series compounds

